AD-A139 967 TOPICAL HAZARD EVALUATION PROGRAM OF CANDIDATE INSECT REPELLENTS AI3-3827.. (U) ARMY ENVIRONMENTAL HYGIENE AGENCY ABERDEEN PROVING GROUND MD J V WADE ET AL. 1/1

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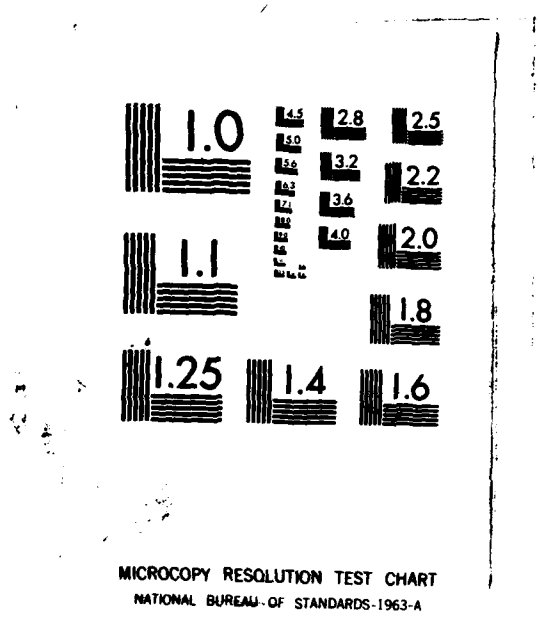

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UNITED STATES ARMY ENVIRONMENTAL HYGIENE AGENCY

ABERDEEN PROVING GROUND, MD 21010

AEHA

TOPICAL HAZARD EVALUATION PROGRAM
OF
CANDIDATE INSECT REPELLENTS
AI3-38273, AI3-38275, AI3-38278, and AI3-38283
US DEPARTMENT OF AGRICULTURE PROPRIETARY CHEMICALS
STUDY NOS. 75-51-0416-84, 75-51-0418-84,
75-51-0420-84, and 75-51-0424-84
FEBRUARY - DECEMBER 1983

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SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

REPORT DOCUMENTATION PAGE		READ INSTRUCTIONS BEFORE COMPLETING FORM
1. REPORT NUMBER 75-51-0416, 0418, 0420, 0424-84	2. GOVT ACCESSION NO. AD-A139967	3. RECIPIENT'S CATALOG NUMBER
4. TITLE (and Subtitle) Topical Hazard Evaluation Program of Candidate Insect Repellents AI3-38273, AI3-38275, AI3-38278, and AI3-38283, US Department of Agriculture Proprietary Chemicals, Study Nos. 75-51-0416-84, 75-51-0418-84, 75-51-0420-84, and 75-51-0424-84, February - December 1983		5. TYPE OF REPORT & PERIOD COVERED Final, February - December 1983 6. PERFORMING ORG. REPORT NUMBER
7. AUTHOR(s) John V. Wade, DVM, CPT(P), VC John G. Harvey, Jr.		8. CONTRACT OR GRANT NUMBER(s) -
9. PERFORMING ORGANIZATION NAME AND ADDRESS Commander US Army Environmental Hygiene Agency Aberdeen Proving Ground, MD 21010		10. PROGRAM ELEMENT, PROJECT, TASK AREA & WORK UNIT NUMBERS
11. CONTROLLING OFFICE NAME AND ADDRESS Commander US Army Health Services Command Ft Sam Houston, TX 72834		12. REPORT DATE February - December 1983 13. NUMBER OF PAGES 7
14. MONITORING AGENCY NAME & ADDRESS(if different from Controlling Office)		15. SECURITY CLASS. (of this report) Unclassified 15a. DECLASSIFICATION/DOWNGRADING SCHEDULE

16. DISTRIBUTION STATEMENT (of this Report)

Approved for public release; distribution unlimited.

17. DISTRIBUTION STATEMENT (of the abstract entered in Block 20, if different from Report)

18. SUPPLEMENTARY NOTES

19. KEY WORDS (Continue on reverse side if necessary and identify by block number)

USDA Proprietary Chemicals	Topical Hazard Evaluation Program	ALD
AI3-38273	Skin Irritation	
AI3-38275	Eye Irritation	
AI3-38278	Photochemical Irritation	
AI3-38283	Guinea Pig Sensitization	

20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

These chemicals did not cause primary irritation of the intact skin and no greater than mild primary irritation of the skin surrounding an abrasion. Chemicals AI3-38273 and AI3-38275 produced mild injury to the cornea and, in addition, some injury to the conjunctiva. Chemical AI3-38278 produced mild injury to the cornea. Chemical AI3-38283 was noninjurious to the eye. These chemicals did not produce photoirritation or sensitization reactions. They demonstrated low to moderate toxicity upon ingestion.

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DEPARTMENT OF THE ARMY
U. S. ARMY ENVIRONMENTAL HYGIENE AGENCY
ABERDEEN PROVING GROUND, MARYLAND 21010

CPT(P) Wade/cvc/AUTOVON
584-3627

REPLY TO ATTENTION OF

HSHB-OT/WP

3 APR 1984

SUBJECT: Topical Hazard Evaluation Program of Candidate Insect Repellents AI3-38273, AI3-38275, AI3-38278, and AI3-38283, US Department of Agriculture Proprietary Chemicals, Study Nos. 75-51-0416-84, 75-51-0418-84, 75-51-0420-84, and 75-51-0424-84, February - December 1983

Executive Secretary
Armed Forces Pest Management Board
Forest Glen Section, WRAMC
Washington, DC 20307

EXECUTIVE SUMMARY

The purpose, essential findings, and major recommendations of the inclosed report follow:

a. Purpose. The purpose of this program is to provide guidance for further entomological testing of the candidate insect repellents AI3-38273, AI3-38275, AI3-38278, and AI3-38283 by means of laboratory animal studies using New Zealand White rabbits, Sprague-Dawley rats, and albino Hartley guinea pigs.

b. Essential Findings. These chemicals did not cause primary irritation of the intact skin and no greater than mild primary irritation of the skin surrounding an abrasion. Chemicals AI3-38273 and AI3-38275 produced mild injury to the cornea and, in addition, some injury to the conjunctiva. Chemical AI3-38278 produced mild injury to the cornea. Chemical AI3-38283 was noninjurious to the eye. These chemicals did not produce photoirritation or sensitization reactions. They demonstrated low to moderate toxicity upon ingestion.

c. Major Recommendations. Recommend that chemicals AI3-38273, AI3-38275, AI3-38278, and AI3-38283 be approved for further testing as candidate insect repellents.

FOR THE COMMANDER:

1 Incl
as (5 cy)

for JOEL C. GLYDOS, M.D.
Colonel, MC
Director, Occupational and
Environmental Health

CF:

HQDA (DASG-PSP) wo incl
Cdr, HSC, (HSCL-P)
Comdt, AHS (HSHA-IPM)
Dir, Advisory Cen on Tox, NRC (2 cy)
USDA, ARS (Dr. Terrence McGovern)
USDA, ARS-Southern Region (3 cy)
Cdr, USAMRDC [SGRD-DPM/LTC(P) Reinert]

A-1

DEPARTMENT OF THE ARMY
U. S. ARMY ENVIRONMENTAL HYGIENE AGENCY
ABERDEEN PROVING GROUND, MARYLAND 21010

REPLY TO ATTENTION OF

HSHB-OT/WP

TOPICAL HAZARD EVALUATION PROGRAM OF CANDIDATE INSECT REPELLENTS AI3-38273, AI3-38275, AI3-38278, and AI3-38283 US DEPARTMENT OF AGRICULTURE PROPRIETARY CHEMICALS STUDY NOS. 75-51-0416-84, 75-51-0418-84, 75-51-0420-84, and 75-51-0424-84 FEBRUARY - DECEMBER 1983

1. AUTHORITY.

a. Letter, US Department of Agriculture - Agricultural Research, Southern Region, Insects Affecting Man and Animals Research Laboratory, Gainesville, Florida, 10 February 1983.

b. Memorandum of Understanding between the US Army Environmental Hygiene Agency; the US Army Health Services Command; the Department of the Army, Office of The Surgeon General; the Armed Forces Pest Control Board; and the Department of Agriculture, Agricultural Research, Science and Education Administrations; titled Coordination of Biological and Toxicological Testing of Pesticides, effective 23 January 1979.

2. REFERENCE. Toxicology Division Topical Hazard Evaluation Program Procedural Guide, US Army Environmental Hygiene Agency (USAEHA), January 1982.

3. PURPOSE. The purpose of this program is to provide guidance for further entomological testing of the candidate insect repellents AI3-38273, AI3-38275, AI3-38278, and AI3-38283, US Department of Agriculture (USDA) Proprietary Chemicals.

4. SUMMARY OF FINDINGS. Hazard evaluations of the candidate insect repellents AI3-38273, AI3-38275, AI3-38278, and AI3-38283, USDA Proprietary Chemicals, were conducted by this Agency using New Zealand White rabbits, Sprague-Dawley rats, and albino Hartley guinea pigs. A tabular presentation of animal toxicity data developed by this Agency follows:*†

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* In conducting the studies described in this report, the investigators adhered to the "Guide for the Care and Use of Laboratory Animals"; US Department of Health, Education, and Welfare; Public Health Service; National Institutes of Health (NIH) Publication No. 80-23, revised 1978, reprinted April 1980.
† The studies reported herein were performed in animal facilities fully accredited by the American Association for the Accreditation of Laboratory Animal Care.

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TABLE. PRESENTATION OF DATA

TEST	RESULTS	INTERPRETATION
SKIN IRRITATION STUDIES		
Rabbits		
Single 24-hour application to intact and abraded skin of New Zealand White rabbits. 0.5 mL technical grade chemical applied to each of six rabbits.	Chemicals AI3-38273, AI3-38275, AI3-38278, and AI3-38283 did not produce primary irritation of the intact skin, and no greater than mild primary irritation of the skin surrounding an abrasion.	USAEHA Category I (ref Appendix A)
EYE IRRITATION STUDIES		
Rabbits		
Single 24-hour application of 0.1 mL technical grade chemical to one eye of each of nine New Zealand White rabbits. Three of the nine rabbits had the eye flushed with warm water for 1 minute, 25 seconds after application.	Chemicals AI3-38273 and AI3-38275 produced mild injury to the cornea and, in addition, some injury to the conjunctiva.	USAEHA Category C (ref Appendix A)
	Chemical AI3-38278 produced mild injury to the cornea.	USAEHA Category B (ref Appendix A)
	Chemical AI3-38283 was noninjurious to the eye.	USAEHA Category A (ref Appendix A)
APPROXIMATE LETHAL DOSE		
Oral		
Rats (male) - No diluent	AI3-38273 $\geq$1,480mg/kg AI3-38275 $\geq$3,333mg/kg AI3-38278 1,480mg/kg AI3-38283 $\geq$2,222mg/kg	These chemicals demonstrated low to moderate oral toxicity. None presented a lethal hazard from accidental ingestion.

TEST	RESULTS	INTERPRETATION
SENSITIZATION STUDIES		
Guinea Pigs (Female)		
Intradermal (ID) injections of 0.1 mL of a minimally irritating concentration of each tested chemical or of dinitrochlorobenzene (DNCB)* in a mixture containing 1 volume propylene glycol and 29 volumes saline.		
Ten test guinea pigs for each chemical were given 10 sensitizing doses over a 3-week period. After a 2-week rest, they were challenged with ID injections of each test chemical.	Challenge doses of chemicals AI3-38273, AI3-38275, AI3-38278, and AI3-38283 did not produce a sensitization reaction.	These chemicals are not expected to produce a sensitization reaction in humans.
Control		
Ten positive control guinea pigs were sensitized over 3 weeks with DNCB. After a 2-week rest, they were challenged with ID injections of DNCB.	Challenge dose of DNCB in positive control guinea pigs produced a marked sensitization reaction in 10 out of 10 guinea pigs.	DNCB produced a marked sensitization reaction, indicating that these guinea pigs respond to sensitizing agents.
PHOTOCHEMICAL SKIN IRRITATION STUDIES		
Rabbits		
A single 0.05 mL application of a 25% (w/v) solution of each chemical and of a 10% (w/v) Oil of Bergamot solution (positive control) in 95% ethyl alcohol was applied to the intact skin of six rabbits. Five minutes after application, the rabbits were exposed to ultraviolet (UV) light (365 nm) for 30 minutes at a distance of 10-15 cm.	These chemicals did not produce photochemical irritation under test conditions.	These chemicals did produce photochemical irritation under test conditions and are not expected to cause photoirritation in humans.
Control		
Following UV exposure of the rabbits, 0.05 mL of test chemicals, positive control and diluent were applied to additional skin areas to serve as unirradiated control sites. Application areas were checked for skin irritation at 24, 48, and 72 hours.	Positive control application and irradiation caused greater irritant effects than produced in unirradiated skin areas.	

* A known skin sensitizer.

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5. CONCLUSION. These chemicals did not produce primary irritation of the intact skin and no greater than mild primary irritation of the skin surrounding an abrasion. Chemicals AI3-38273 and AI3-38275 produced mild injury to the cornea and, in addition, some injury to the conjunctiva. Chemical AI3-38278 produced mild injury to the cornea. Chemical AI3-38283 was noninjurious to the eye. These chemicals did not produce sensitization or photoirritation reactions. They demonstrated low to moderate toxicity upon ingestion. These studies were monitored by Analytical Quality Assurance Office (see Appendix B).

6. RECOMMENDATION. Recommend that chemicals AI3-38273, AI3-38275, AI3-38278, and AI3-38283 be approved for further testing as candidate insect repellents.

JOHN V. WADE, DVM
CPT(P), VC
Laboratory Animal
Veterinary Officer
Toxicology Division

JOHN G. HARVEY, JR
Biological Laboratory Technician
Toxicology Division

APPROVED:
MAURICE H. WEEKS
Chief, Toxicology Division

TOPICAL HAZARD EVALUATION PROGRAM
DEFINITIONS OF CATEGORIES OF COMPOUNDS BEING
CONSIDERED FOR ACUTE SKIN APPLICATION

CATEGORY I - Compounds producing no primary irritation of the intact skin or no greater than mild primary irritation of the skin surrounding an abrasion. (INTERPRETATION: No restriction for acute application to the human skin.)

CATEGORY II - Compounds producing mild primary irritation of the intact skin and the skin surrounding an abrasion. (INTERPRETATION: Should be used only on human skin found by examination to have no abrasions or may be used as a clothing impregnant.)

CATEGORY III - Compounds producing moderate primary irritation of the intact skin and the skin surrounding an abrasion. (INTERPRETATION: Should not be used directly on the skin without a prophetic patch test having been conducted on humans to determine irritation potential to human skin. May be used without patch testing, with extreme caution, as clothing impregnants. Compound should be resubmitted in the form and at the intended use concentration so that its irritation potential can be reexamined using other test techniques on animals.)

CATEGORY IV - Compounds producing moderate to severe primary irritation of the intact skin and of the skin surrounding an abrasion and, in addition, producing necrosis, vesiculation, and/or eschars. (INTERPRETATION: Should be resubmitted for testing in the form and at the intended use concentration. Upon resubmission, its irritation potential will be reexamined using other test techniques on animals, prior to possible prophetic patch testing in humans, at concentrations which have been shown not to produce primary irritation in animals.)

CATEGORY V - Compounds impossible to classify because of staining of the skin or other masking effects owing to physical properties of the compound. (INTERPRETATION: Not suitable for use on humans.)

EYE CATEGORIES:

A. Compounds noninjurious to the eye. INTERPRETATION: Irritation of human eyes is not expected if the compound should accidentally get into the eyes, provided it is washed out as soon as possible.

B. Compounds producing mild injury to the cornea. INTERPRETATION: Should be used with caution around the eyes.

C. Compounds producing mild injury to the cornea, and in addition some injury to the conjunctiva. INTERPRETATION: Should be used with caution around the eyes and mucosa.

D. Compounds producing moderate injury to the cornea. INTERPRETATION: Should be used with extreme caution around the eyes.

E. Compounds producing moderate injury to the cornea, and in addition producing some injury to the conjunctiva. INTERPRETATION: Should be used with extreme caution around the eyes and mucosa.

F. Compounds producing severe injury to the cornea and to the conjunctiva. INTERPRETATION: Should be used with extreme caution. It is recommended that use be restricted to areas other than the face.

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APPENDIX B

ANALYTICAL QUALITY ASSURANCE

The Analytical Quality Assurance Office certifies the following:

a. These studies were conducted in accordance with:

(1) Standing Operating Procedures developed by the Toxicology Division, USAEHA.

(2) Title 21, Code of Federal Regulations (CFR), 1983 rev, Part 58, Good Laboratory Practice for Nonclinical Laboratory Studies.

(3) Final Rule, Pesticide Programs; Good Laboratory Practice Standards; 48 Federal Register (FR) 53963-539691, 29 November 1983.

b. Facilities were inspected during its operational phase to ensure compliance with paragraph a above.

c. The information presented in this report accurately reflects the raw data generated during the course of conducting these studies.

PAUL V. SNEERINGER, Ph.D.
Chief, Analytical Quality
Assurance Office